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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,286	12/07/1999	MICHAEL GROLL	P564-9039	3782

7590 01/27/2003

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,286	GROLL ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Petition grant* .

DETAILED ACTION

Applicants' arguments, filed 20 November 2002, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 21-27 are currently pending.

The indicated allowability of claims 21, 22, 24, and 27 is withdrawn upon further consideration of the claimed subject matter.

Drawings

The petition to accept color drawings submitted 5 December 2001 has been granted.

Claim Rejections - 35 USC § 112

Claims 21-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of

experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to identify and isolate proteosome inhibitors based upon some crystallized fraction of a cell extract. However, for the reasons discussed below, this constitutes undue experimentation.

b) The specification provides examples for known proteosomes in the art, such as the 20S proteosome from *Archaebacterium Thermoplasma acidophilum* (page 1, 3rd paragraph) and the eukaryotic proteosome, 20S, from *Sacchromyces cerevisiae* (page 2, 2nd paragraph). Many other examples from the art are given on pages 3-5. However, no crystallographic data have been described for eukaryotic proteosomes.

c) The specification provides working examples of protein preparations from *Saccharomyces cerevisiae* (page 11, example 1). The specification also provides crystallization procedures and analysis techniques, without ever providing specific coordinates relating to any one crystal of interest. Structural information for some proteosome components is described, however, this is not in conjunction with a crystal product.

d) The invention is drawn to methods of finding proteosome inhibitors using crystal data. However, the instant specification provides no indication whatsoever, about what has been crystallized, let alone any coordinates to a particular structure. There would be no possible way to reproduce the crystals of the specification in order to practice the method of the claims. Furthermore, after the fraction isolation in claim 21, and crystallization of fractions, analysis of

the crystallized structures is to be performed. However, the step of "analyze" provides no guidance as to what to model for in order to find supposed inhibitors of proteosomes. In claim 22 the structure analysis of the crystallized fractions is done by comparison of the data to known proteosomes. However, according to the specification, no proteosomes from eukaryotes have been crystallized and prokaryotic proteosome homology is too low (page 2). Once more, analysis of structure does not give guidance on how to identify inhibitors. In claim 23, the structure of the crystallized fractions is compared to regions of subunits. However, what data are used to do this? No coordinates are identified.

e) and g) It would have been well known in the protein crystallization is unpredicatable. It is mainly by trial-and-error that proper conditions are attained for crystallization. It is even noted in the art for eukaryotic proteosomes, that this is a very difficult process (see specification at page 2, 2nd paragraph; page 3, 3rd paragraph). It would have been well known in the art that the homologous proteins from different sources cannot be easily crystallized using the same techniques and/or conditions and results might yield completely different crystals (see claim 25). See for example, Jan Drenth (Chapter 1, pages 1-9 of "Principles of Protein X-ray Crystallography", 1994, Springer-Verlag New York, Inc.)

f) The skill of those in the art of crystallography is high, however, the science of obtaining the exact crystal is still uncertain.

h) The claims are broad because they do not identify a particular crystal product that would be used in the identification of proteosome inhibitors. Nor do the claims elucidate how identification of an inhibitor would be performed.

The skilled practitioner would first turn to the instant specification for guidance to practice these methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that such predictions are highly unpredictable, and require substantial additional work and research. Finally, said practitioner would turn to trial and error experimentation to determine crystal structure and steps to identify proteosome inhibitors. Such represents undue experimentation.

Claims 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21-27 require the testing of a biological activity of the fractions. However, there is no indication about what biological activity is being tested in each of the fractions. Furthermore, is the same biological activity being tested or are separate biological activities being tested?

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800

AU1631

January 24, 2003

Lori A. Clow, Ph.D.
Art Unit 1631

Lori A. Clow